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Attorney's Docket No. 5800-8A (35800/185816) PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| In re: | Glucksmann *et al.* | Confirmation No. | 6988 |
| Appl. No.: | 09/383,745 | Group Art Unit: | 1646 |
| Filed: | August 26, 1999 | Examiner: | Eliane M. Lazar-Wesley |
| For: | 14926 RECEPTOR, A NOVEL G-PROTEIN COUPLED RECEPTOR | | |



November 25, 2002

Box AF
Commissioner for Patents
Washington, DC 20231

**APPELLANT'S REPLY BRIEF TRANSMITTAL**
**(PATENT APPLICATION – 37 C.F.R. § 1.193(b))**

Transmitted herewith, in triplicate, is the APPELLANT'S REPLY BRIEF in this application, with respect to the Examiner's Answer mailed on October 2, 2002.

Respectfully submitted,

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**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Box AF, Commissioner for Patents, Washington, DC 20231 on November 25, 2002.

Nora C. Martinez

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**APPELLANT'S REPLY BRIEF**

Sir:

This Reply Brief is filed in response to the "Examiner's Answer" mailed October 2, 2002.

**INTRODUCTION**

In the Examiner's Answer mailed October 2, 2002, the Examiner presented new arguments relating to Issues 1, 2, and 3 of Appellants' Appeal Brief mailed June 21, 2002. Accordingly, Appellants here respond to the new arguments presented in the Examiner's Answer.

*Issue 1--Whether the invention of claims 32-59 has utility under 35 U.S.C. §101 and thus is enabled under 35 U.S.C. §112, first paragraph.*

**I. The 14926 receptor has specific, substantial, and credible utility.**

The pending claims of the instant invention are drawn to methods of modulating the activity of a rhodopsin family G-protein coupled receptor (GPCR) and methods of identifying a compound that modulates the activity of a rhodopsin family GPCR. Appellants have asserted a specific, substantial, and credible utility for the claimed

methods. Specifically, Appellants have shown that rhodopsin family GPCRs and methods for their use in drug screening have real world utility because members of this family of receptors have historically been among the most successful drug targets. In fact, members of the rhodopsin family or receptors are the molecular target of more than 50% of all prescription drugs. Attwood (2001) *Trends in Pharmacological Science* 22:162-165. The utility asserted for the methods of the present invention are based on the unique properties of rhodopsin family GPCRs, including their modulation by small molecules, their ability to mediate intracellular signal transduction, and their resulting important role as therapeutic targets.

For example, rhodopsin family GPCRs, including the rhodopsin family GPCR of the present invention, have utility in selectivity screening of candidate drugs that target GPCRs. It is well known in the art that drugs that bind selectively to their molecular target are highly preferred over those that bind to structurally related molecules, as the selective compounds are far less likely to have unwanted side effects in clinical use. Thus, an important component of any drug development strategy is determining the selectivity of the candidate drug for the molecular target of interest over structurally related polypeptides. The goal of selectivity screening is to identify a drug that binds to the molecular target of interest, but not to the structurally related molecules. The effectiveness of selectivity screening increases in proportion with the number of structurally related polypeptides screened, because a drug that binds specifically to the molecular target of interest but not to any known structurally related polypeptides is less likely to have unwanted side effects when used in drug therapy.

Appellants have asserted that the claimed methods of the present invention are useful in selectivity screening for compounds that bind specifically to rhodopsin family GPCRs. Appellants have cited a reference, Goodwin *et al.* (2000) *Molecular Cell* 6:517-526, provided as Appendix C with Appellants' Appeal Brief mailed June 21, 2002, that shows the use of orphan nuclear receptors in a screening assay for compounds that specifically bind to the therapeutic target FXR. The reference demonstrates the utility of orphan receptors (*i.e.*, receptors for which endogenous ligands have not been identified) in selectivity screening, and further demonstrates that the structural similarity of the

orphan receptor to the target protein confers a real world utility to the orphan receptor in the absence of a knowledge of the orphan receptor's endogenous ligand or biological function.

Appellants have also demonstrated that the methods of claims 32-59 are useful in screening for drugs that modulate the activity of the 14926 GPCR. Appellants have cited Stadel *et al.* (1997) *Trends in Pharmacology* 18:430-436, provided as Appendix B with Appellants' Appeal Brief mailed June 21, 2002, to demonstrate that those of skill in the art view orphan GPCRs as providing an immediate benefit in the reverse molecular pharmacology approach to drug screening, where a full-length cloned receptor, rather than a ligand having an unknown molecular target, is the starting point of the drug discovery process. The Stadel *et al.* reference states that those of skill in the art recognize the benefit of using a reverse pharmacology approach to screening for drugs that modulate GPCRs because

> [T]he potential reward of using this approach is that resultant drugs naturally will be pioneer or innovative discoveries, and a significant proportion of these unique drugs may be useful to treat diseases for which existing therapies are lacking or insufficient.

Stadel *et al.*, page 434. Thus, this reference shows that those of skill in the art recognize the real-world benefit of methods of screening using orphan GPCRs.

Accordingly, Appellants have demonstrated that the 14926 receptor is a member of the rhodopsin family of GPCRs, a family of cell membrane receptors that bind small molecules to mediate signal transduction pathways and that have historically been among the most successful drug targets. Because of these properties, which are specific to rhodopsin family G-protein coupled receptors, those of skill in the art recognize that the identification of novel orphan rhodopsin family G-protein coupled receptors has real-world value in the pharmaceutical research field as a tool in drug screening and selectivity screening, even in the absence of a knowledge of an endogenous ligand, precise biological function, or disease association for this receptor.

**II. The "Utility Examination Guidelines" require a *specific* utility, not a *unique* utility.**

*1. The utilities asserted by the Appellants for the methods of claims 32-59 are specific utilities, not general utilities.*

The Examiner has argued that the use of the 14926 receptor sequence in drug screening and selectivity screening is not a specific utility because, "it does not rely on a particular characteristic of the instant 14926 gene, but rather relies on features shared by many diverse GPCRs." October 2, 2002 Examiner's Action, page 9. The Examiner also argues that "using all members of the GPCR family in selectivity screening does not impart a specific utility to this one species." October 2, 2002 Examiner's Action, page 7. Accordingly, the Examiner has not accepted the specific, substantial utility conferred on the 14926 receptor as a member of the rhodopsin family of GPCRs, but instead, has required the Appellants to assert a utility that is unique to the 14926 receptor in order to establish the patentable utility of the claimed methods.

The standard for assessing specific utility applied by the Examiner is at odds with the "Utility Examination Guidelines," which provide that "[w]hen a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein." 66 Fed. Reg. 1092, 1096 (2001). This statement from the "Utility Examination Guidelines" makes it clear that when a sequence is shown to encode a polypeptide belonging to a family of proteins that share a common utility, the common utility is not considered to be non-specific merely because it is shared by all the members of the protein family. Thus, the "Guidelines" do not require an applicant to demonstrate that a claimed polypeptide is the only polypeptide having the asserted utility in order to meet the requirements of 35 U.S.C. § 101.

The Examiner argues that Appellants' arguments are unpersuasive because "G-protein coupled receptors belong to a large family having very different ligands and functions . . . where there is great functional diversity in a structurally related class of compounds, the class cannot be used to predict a utility for a new compound that fits in

the class by structural similarity." October 2, 2002 Examiner's Answer, page 6. However, Appellants have not argued that all rhodopsin family GPCRs share a common utility because they bind to the same ligand or have an identical physiologic function. Rather, Appellants have shown that all rhodopsin family GPCRs share a common utility because of their structural similarity with therapeutically important molecular targets and their G-protein mediated signal transduction activity. Thus, the rhodopsin family of G-protein coupled receptors is not diverse with respect to the utility asserted for the claimed methods.

*2. Example 10 of the "Revised Interim Utility Guidelines Training Materials" demonstrates that a unique utility is not required in order to establish patentable utility.*

Appellants have cited Example 10 of the "Revised Interim Utility Guidelines Training Materials" to demonstrate that sequence identity with a class of proteins having a specific and substantial utility may be used to establish the specific and substantial utility of a polypeptide, and that a utility that is unique to the claimed polypeptide is not required to establish patentable utility. Example 10 of the "Revised Interim Utility Guidelines Training Materials" is directed to a nucleic acid encoding a polypeptide having a high level of sequence identity with DNA ligases. If the policy set forth in the Examiner's Answer as described above were followed, the polypeptide claimed in Example 10 of the "Revised Interim Utility Guidelines Training Materials" would be rejected for lack of utility because the well-established utility in this example is based on the claimed polypeptide's ligase activity and this utility is shared with all members of the ligase family of proteins, rather than being unique to the newly-identified ligase. Instead, however, it is concluded in the analysis of this example that the claimed ligase has patentable utility. The patentable utility is demonstrated *because* the ligase can be used for the same purpose as other members of the ligase family of proteins, not in despite this fact.

Similarly, Appellants have shown that the 14926 receptor is a member of the rhodopsin subfamily of GPCRs. Members of this family of receptors bind small molecules and mediate signal transduction via phosphatidylinositol-mediated pathways or

cyclic AMP-mediated pathways, and these unique properties have historically made GPCRs among the most successful drug targets as described above. The utilities asserted for the claimed invention in drug screening and selectivity screening are based on the properties shared by the rhodopsin family of GPCRs. These properties are shared by and specific to members of the rhodopsin family of GPCRs. Accordingly, the utility asserted for the claimed screening methods is a utility specific to rhodopsin family GPCRs, not a general utility applicable to all proteins, or even to all membrane receptors.

*3. The facts of the instant application are not factually analogous to Example 12 of the "Revised Interim Guidelines Training Materials."*

The Examiner argues that "[a] more accurate example is Example 12, that deals with receptors and a method of identifying materials which bind to receptor A." October 2, 2002 Examiner's Answer, pages 9-10. In fact, the claimed invention of the present application can be factually distinguished from that of Example 12 of the "Revised Interim Guidelines Training Materials" on several grounds. Example 12 of the "Training Materials" is directed to a polypeptide that binds a ligand, X, of unknown function. In this example, it is specifically stated that the polypeptide has been characterized as a receptor based solely on the fact that it was isolated from a cell membrane and binds ligand X. Unlike the claimed invention of this application, the claimed polypeptide of Example 12 demonstrates no significant sequence similarity with a protein of known function, and is therefore found not to possess a well-established utility.

As described above, Example 10 of the "Revised Interim Utility Guidelines Training Materials," which is directed to a sequence with a high degree of sequence similarity with a DNA ligase, more accurately represents the situation found in the instant application. Like Example 10 (and unlike Example 12), the claimed invention has been shown to share a high degree of sequence similarity with a protein of known function. In Example 10, the claimed protein shares sequence similarity with a protein having ligase activity, while in the present example the claimed protein shares sequence similarity with proteins having G-protein mediated signal transduction activity. Like Example 10 (and unlike Example 12), the protein of known function has a well-established utility. The well-established utility is the use as a tool in drug screening. While the asserted utility of

the polypeptide of Example 12 relates to the identification of agents and the generation of antibodies that bind this polypeptide with no structural similarity to polypeptides of known utility, the utility of the present claims is based on the well-established utility of the protein family with which the claimed sequence shares a high degree of sequence similarity.

**III. No further research is required to identify or confirm a specific utility for the methods of claims 32-59.**

*1. The Manual of Patent Examining Procedure provides that claims should not be rejected for lack of patentable utility because the claimed invention is useful in a research setting*

Appellants have asserted that the methods of claims 32-59 have specific utility in drug screening and selectivity screening for compounds that target rhodopsin family GPCR. The Examiner argues that "[t]here is clearly a requirement for further research on the instant receptor in order to determine the specific use." October 2, 2002 Examiner's answer, page 8. However, the evidence presented by the Appellants demonstrates that the claimed methods have specific utility, and that no further research is required to confirm this specific utility.

The *Manual of Patent Examination Procedure* provides that:

> Confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, *screening assays*, and nucleotide sequencing techniques have a clear, specific, and unquestionable utility (e.g. they are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense.

*Manual of Patent Examination Procedure* § 2107.01 (8th ed. 2001), emphasis added. Accordingly, Appellants' asserted utilities for the methods of claims 32-59 in drug screening and selectivity screening are not insubstantial or non-specific merely because these utilities are operable in a laboratory setting.

The *Manual of Patent Examination Procedure* further provides that "Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify and reasonably confirm." *Id.* Accordingly, if the Appellants assert a specific, substantial utility for the claimed invention, and additional research is not required in order to identify and confirm this utility, then the claims should not be rejected on the grounds that they lack patentable utility. Thus, if those of skill in the art can use the invention in a way that provides an immediate benefit, the requirement for patentable utility is met.

*2. No further research is required to confirm the asserted utility for the methods of claims 32-59 in selectivity screening.*

Appellants have provided evidence demonstrating the real world utility of orphan receptors in the drug screening process as viewed by those of skill in the art. For example, the methods of claims 32-59 have specific, substantial, and credible utility in selectivity screening for drugs targeting rhodopsin family GPCRs as described *supra*. The purpose of selectivity screening is not to identify a specific utility for the 14926 GPCR as alleged by the Examiner. Rather, in selectivity screening the 14926 receptor serves as a research tool for use in the identification of compounds that bind specifically to therapeutic targets that are rhodopsin family GPCRs. Such research tools provide immediate benefit to those of skill in the art because they play an important role in the development of selective therapeutic agents. Accordingly, the asserted utility meets the standard set forth in *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980), where the court held that "[p]ractical utility is a shorthand way of attributing 'real-world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." 206 USPQ at 883.

Furthermore, no additional research to identify a disease association, biological role, or endogenous ligand is required in order for one of skill in the art to use the claimed methods as asserted by the Appellants. Rather, the methods have specific utility because the 14926 receptor is a member of a family of receptors containing a number of

important therapeutic targets. The use of such receptors in selectivity screening provides an immediate benefit to the public regardless of whether a disease association, biological role, or ligand for the 14926 receptor is identified.

*3. No further research is required to confirm the asserted utility for methods of claims 32-59 receptors in drug screening.*

Appellants have presented evidence demonstrating that those of skill in the art consider the identification of a novel orphan GPCR to provide immediate benefit in other types of drug screening. Stadel *et al.* (1997) *Trends in Pharmacological Science* 18:430-36, described *supra*, demonstrate that advances in molecular biology have led to dramatic changes in the way therapeutic compounds are identified. The Stadel *et al.* reference teaches that the availability of sequences encoding novel orphan GPCRs has led to a new pharmaceutical research paradigm based on a reverse molecular pharmacology approach to drug discovery. In the reverse molecular pharmacology approach, it is a full-length cloned receptor, rather than a ligand having an unknown molecular target, that is the starting point of the drug discovery process. *See*, Figure 2 of Stadel *et al.*

Accordingly, further research to identify a ligand for the 14926 receptor is not required in order to confirm that the claimed methods may be used as described by Stadel *et al.* Furthermore, Stadel *et al.* teach that the rewards of using a reverse molecular pharmacology approach to drug discovery, based on the identification of novel orphan GPCRs, is that "resultant drugs naturally will be pioneer or innovative discoveries, and a significant proportion of these unique drugs may be useful to treat disease for which existing therapies are lacking or insufficient." Stadel *et al.*, page 434. Thus, this reference demonstrates that those of skill in the art consider orphan GPCRs to provide an immediate benefit in drug screening. Therefore, further research to identify a physiologic role, endogenous ligand, or disease association for the 14926 receptor are not required to use the claimed methods as asserted.

The Examiner argues that because Stadel *et al.* teach that the reverse molecular pharmacology strategy is more risky than a traditional approach to drug discovery, further research would be required to determine if the claimed methods of the present invention have utility. This argument is contrary to the teachings of Stadel *et al.*, because

when the Stadel *et al.* reference is considered in its entirety, it is clear that its primary teaching is not that the process of using orphan GPCRs in a reverse molecular pharmacological approach to drug discovery is insurmountably difficult and should not be attempted, but rather that the reverse molecular pharmacology using orphan GPCRS is already being actively pursued because "the pharmaceutical industry has recognized the power of genomics to provide it with new and unique drug targets." Stadel *et al.*, page 436. Accordingly, this reference provides evidence that those of skill in the art recognize the real-world utility of orphan GPCRs.

*4. The facts of the present case are distinguishable from those of Brenner v. Manson.*

The Examiner cites *Brenner v. Manson*, 148 USPQ 689 (S.Ct., 1966) for the Court's statement that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." However, this statement is inapposite to the facts of the present case, because Appellants have asserted a specific utility for the methods of the present invention. The claimed methods are not the object of use-testing for the reasons described above.

Furthermore, the facts of the present case can be readily distinguished from those in *Brenner*. In *Brenner*, the claims at issue were directed to a process for making certain steroidal compounds. During the prosecution of the application, Mr. Brenner asserted that the use of the steroidal compounds produced by his process were useful as potential tumor inhibiting agents based on the fact that a structural homologue of these compounds had been shown to have anti-tumor activity. However, structural similarities between steroidal compounds are not know in the art to provide a sufficient likelihood that these compounds will have similar functional characteristics. Indeed, Mr. Brenner recognized that the presumption that adjacent homologues have the same utility had been challenged in the steroid field because of "a greater known unpredictability of compounds in that field." 148 USPQ at 694. In finding that the claims lacked patentable utility, the Court made it clear that the unpredictability of this particular field was important to their finding of lack utility for the claimed invention, stating, "[i]n these circumstances, and in

this technical area, we would not overturn the finding of the Primary Examiner, affirmed by the Board of Appeals and not challenged by the CCPA." 148 USPQ at 694.

In contrast, the utility of the claimed methods of the present invention are based on the fact that the 14926 receptor is a rhodopsin-family GPCR. As described elsewhere herein and illustrated by several examples, members of the rhodopsin family of GPCRs have a well-established, specific utility in drug screening and selectivity screening. Accordingly, Appellants have established that the methods of claims 32-59 have patentable utility, and there is not need to perform further research to identify or confirm a utility for the claimed invention.

## IV. The Examiner has not established a *prima facie* case of no utility.

The "Examination Guidelines for the Utility Requirement," MPEP § 2107, set forth the elements required to establish a *prima facie* case of no utility as follows:

> Where the asserted utility is not specific or substantial, a *prima facie* showing must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The prima facie showing must contain the following elements:
>
> (i) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established;
>
> (ii) Support for factual findings relied upon in reaching this conclusion; and
>
> (iii) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

MPEP § 2107 (8th ed. 2001). These guidelines are in accordance with *In re Brana*, 34 USPQ2d 1437 (Fed. Cir. 1995), where the Federal Circuit held that, "[o]nly after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the Applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility." 34 USPQ2d at 1441.

The Examiner argues that *Brana* is not applicable because "what is challenged here is not that one would or would not believe in a potential utility, but what is challenged is that Appellants have not provided a substantial and specific utility for their invention." October 2, 2002 Examiner's Action, page 11. However, the court in *Brana* did not hold that the Examiner had the burden of establishing a *prima facie* of no utility only when the grounds of the rejection was that the asserted utility is not credible. Rather, the court in *Brana* held that "the PTO has the initial burden of challenging the presumptively correct assertion of utility in the disclosure." 34 USPQ2d at 1441. Thus, under MPEP § 2107 and the supporting case law, the Examiner has the burden of establishing a *prima facie* case of no utility regardless of whether the rejection is based on the grounds that the asserted utility is not credible or the grounds that the asserted utility is not specific and substantial.

In the present case, Appellants have asserted that the claimed methods are useful in drug screening and selectivity screening for candidate drugs that specifically target GPCRs. The Examiner has rejected the claims under 35 U.S.C. § 101 on the grounds that the asserted utility is not specific and substantial, and that further research is required to demonstrate the patentable utility of this receptor. However, contrary to the requirements of MPEP § 2107 and *Brana*, the Examiner has not provided the factual findings or evidence relied on in reaching this conclusion.

Furthermore, Appellants have provided evidence demonstrating the specific and substantial utility of orphan receptors in the drug screening process. As described above, the Appellants have provided evidence showing that orphan receptors play a critical role in identifying agonists and antagonists that bind to therapeutic targets but not to structurally-related molecules. The Appellants have also provided evidence showing that because the rhodopsin family of G-protein coupled receptors contains a number of key drug targets, members of this family share a real world use in drug screening including selectivity screening of drugs. The Examiner has not provided any factual findings or evidence to demonstrate that a knowledge of the precise physiological function of the receptor is required in order to use the invention in the manner asserted by the Appellants, or that a person of ordinary skill in the art would find that the claimed

invention lacked specific and substantial utility in selectivity screening and drug screening in the absence of a knowledge the precise biological role of the 14926 receptor.

In the Examiner's Answer, the Examiner argues that the Appellants have not demonstrated that the 14926 receptor functions as a G-protein coupled receptor. October 2, 2002 Examiner's Answer, page 11. However, no evidence is presented to demonstrate that one of skill in the art would doubt that the 14926 receptor functions as a GPCR. Furthermore, this statement contradicts statements made in the Office Action mailed December 14, 2001, in which the Examiner states that the claims are not rejected "under the grounds that 14926 might be a G-protein coupled receptor . . . but rather than at the time the application was filed, appellants have not provided a specific and substantial utility for the gene." December 14, 2001 Office Action, page 4. Appellants note that such shifts in the Examiner's reasoning make it difficult to determine and address the grounds of the rejection. As stated by the court in *In re Oetiker*,

> The examiner cannot sit mum, leaving the applicant to shoot arrows into the dark hoping to somehow hit a secret objection harbored by the examiner. The "prima facie case" notion . . .seemingly was intended to leave no doubt among examiners that they must state clearly and specifically any objections (the prima facie case) to patentability, and give the applicant fair opportunity to meet those objections with evidence and arguments.

*In re Oetiker*, 24 USPQ2d 1443 (Fed. Cir. 1992), *J. Plager, concurring.*

Under the Guidelines, "[t]he examiner's decision [with respect to patentable utility] must be supported by a preponderance of all the evidence of record," MPEP § 2107.02 (8th ed. 2001), *citing In re Oetiker*, 24 USPQ2d 1443 (Fed. Cir. 1992). In the present case, Appellants' references constitute the only evidence of record demonstrating the view of those of skill in the art regarding the utility of methods of screening using orphan rhodopsin family GPCRs. Accordingly, the preponderance of the evidence supports Appellants' asserted utility.

**V. The asserted utility for the invention of claims 32-59 meets the standard set forth in the USPTO "Utility Examination Guidelines" and the supporting case law.**

The Examiner has argued that the Appellants must identify a 14926 receptor ligand, physiologic function, or disease association in order to satisfy the utility requirement under 35 U.S.C. § 101 and has refused to accept the specific, substantial, and credible utilities asserted by the Appellants despite the fact that these asserted utilities do not require a knowledge of the 14926 ligand or physiologic function in order to be operable. The requirements for utility set forth in the Examiner's Answer demonstrate that the Examiner is applying an improperly heightened utility standard to the present invention. This heightened utility standard is at odds with the standard set by the "Utility Examination Guidelines" and the applicable case law.

The USPTO "Utility Examination Guidelines" state, "[a]n applicant need only provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement." 66 Fed. Reg. 1092, 1098 (2001). This standard is consistent with *Cross v. Iizuka*, 753 F.2d 1040 (Fed. Cir. 1985) in which the court held that "[w]hen a properly claimed invention meets at least one stated objective, utility under §101 is clearly shown." Thus, the Examiner's utility rejection must necessarily depend on the invalidity of each of Appellants' asserted uses.

The PTO guidelines state, "[a] rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial, and credible by a person of ordinary skill in the art in view of all evidence of record" 66 Fed. Reg. at 1098. Further, the guidelines state, "[c]redibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record...that is probative of the applicant's assertions." *Id.* Appellants have demonstrated that one of ordinary skill in the art would find the present invention useful for selectivity screening of compounds that target rhodopsin family GPCRs as described above and thus the utility standard is met.

For these reasons, the rejection of claims 32-59 under 35 U.S.C. § 101 should be reversed.

***Issue 2—Whether the invention of claims 32-59 is enabled under 35 U.S.C. § 112, first paragraph.***

The Examiner has maintained the rejection of claims 32-59 under 35 U.S.C. § 112, first paragraph, on the grounds that these claims recite a step of determining whether a test compound modulates the activity of a 14926 polypeptide but have not disclosed which activity to measure. Appellants have demonstrated that the specification provides guidance regarding G-protein mediated signaling pathways, including pathways mediated by phophatidylinositol turnover and pathways mediated by cyclic AMP turnover and metabolism, and that methods for assaying these signal transduction pathways are well known in the art. Accordingly, based on the guidance provided in the specification, one of skill in the art would be able to determine whether a test compound modulates the activity of a 14926 polypeptide as recited in the claim.

In the Examiner's Answer, the Examiner newly argues that Appellants' arguments are not persuasive because "although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims." October 2, 2002 Examiner's Answer, page 13. This grounds for the rejection is difficult to address, because it seems to suggest that all of the guidance provided in the specification regarding G-protein mediated signal transduction pathways must also be recited in the claims. Appellants are aware of no authority, binding or otherwise, that have held that the claims must specifically recite all the guidance required to make use the claimed invention in order to satisfy the enablement requirement under 35 U.S.C. § 112, first paragraph.

The Examiner also argues that some GPCRs are capable of sending signals through both G-proteins and alternative signaling molecules. However, the claims at issue specifically recite that the proteins having G-protein mediated signal transduction activity, and that the specification provides sufficient guidance to allow one of skill in the art to assay for this activity. Accordingly, enablement commensurate with the scope of the claims is provided.

For these reasons, the rejection of claims 32-59 under 35 U.S.C. §112, first paragraph, for lack of enablement should be reversed.

*Issue 3—Whether the invention of claims 37-46 and 54-57 meets the written description requirement set forth in 35 U.S.C. § 112, first paragraph.*

**I. The inventions of claims 37-46 and 54-57 is sufficiently described under the "Written Description Guidelines" and supporting case law.**

The Examiner has maintained the rejection of claims 37-46 and 54-57 under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not provide a sufficient written description of the polypeptides used in the methods of these claims. Appellants have demonstrated that the Examiner is applying an incorrect legal standard in determining whether the methods of claims 37-46 and 54-57 are sufficiently described. In the Examiner's Answer mailed October 2, 2002, the Examiner maintains the rejection for insufficient written description under 35 U.S.C. § 112, first paragraph, but does not address Appellants' arguments regarding the legal standard for written description of a genus of polypeptides.

The Examiner continues to argue that the Appellants must disclose which mutations and substitutions would result in a functional variant of the 14926 receptor. Thus the Examiner requires that the specification disclose the sequence of each variant falling within the structural and functional limitations set forth in the claims in order to provide a sufficient written description for the claimed genera of sequences. However, this requirement is not supported by the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement," 66 Fed. Reg. 1099 (2001), and the supporting case law.

The "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement" state that genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying characteristics , *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. Appellants submit that the written description provided for the polypeptides

recited in claims 37-46 and 54-57 meets this requirement. The claims recite the identifying structural characteristics that define each genus of nucleotide sequences or amino acid sequences. Claims 37 and 54 recite polypeptides comprising an amino acid sequence having at least 70, 80%, or 90% sequence identity with amino acid sequence shown in SEQ ID NO:1. Claims 42 and 56 recite polypeptides comprising the amino acid sequence of a sequence variant of the amino acid sequence shown in SEQ ID NO:1, where the sequence variant is encoded by a nucleotide sequence that hybridizes to the nucleotide sequence shown in SEQ ID NO:2 under the specified stringent conditions. The structural limitations in these claims provide the identifying characteristics of the claimed genera of proteins and therefore meet the requirements set forth in the "Guidelines."

Claims 37-46 and 54-57 also meet the standard for written description established in *Regents of the University of California v. Eli Lilly & Co*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing Fiers v. Revel 984 F.2d 1164 (Fed. Cir. 1993). The structural limitations recited in claims 37-46 and 54-57 are sufficient to distinguish the claimed nucleotide sequences from other materials and thus sufficiently define the claimed genus.

The Federal Circuit in *Lilly* further held that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." 119 F.3d at 1569. The written description provided for the genera of sequences recited in claims 37-46 and 54-57 meets this requirement because these claims recite the identifying structural characteristics that define each genus of polypeptides. Specifically, these claims encompass only amino acid sequences having at least 70, 80%, or 90% sequence identity with amino acid sequence shown in SEQ ID NO:1, and amino acid sequences of sequence variants of the amino acid

sequence shown in SEQ ID NO:1, where the sequence variant is encoded by a nucleotide sequence that hybridizes to the nucleotide sequence shown in SEQ ID NO:2 under the specified stringent conditions.

The Appellants have further provided the functional characteristics that distinguish the claimed sequences of the genus. Claims 37, 42, 54, 56, and their dependent claims are drawn to a genus of polypeptides having G-protein mediated signal transduction activity. Thus, each genus of sequences recited in claims 37-46 and 54-57 has been described by its identifying structural and functional characteristics, and one of skill in the art would recognize that the inventors were in possession of the claimed invention. Therefore, the requirement for a written description of the claimed invention under 35 U.S.C. § 112, first paragraph, is met.

**II. The present invention is analogous to Example 14 of the "Revised Interim Written Description Guidelines Training Materials."**

Appellants have shown that the facts of the present situation are analogous to those of Example 14 of the " Revised Interim Written Description Guidelines Training Materials," available at www.uspto.gov/web/menu/written.pdf. This example demonstrates that when the structural and functional features of the sequences encompassed by a genus of sequences are described, the description of the genus meets the requirements of 35 U.S.C. § 112, first paragraph.

In the Examiner's Answer, the Examiner argues that the facts of Example 14 of the "Training Materials" are not analogous to the facts of the present situation because in Example 14 "the function is well defined." October 2, 2002 Examiner's Answer, page 14. However, Example 14 is in fact analogous to the facts of the present situation, because the function recited in claims 37-46 and 54-57 is also well defined. The claims recite that the encompassed polypeptides have G protein mediated signal transduction activity, and this activity is described in the specification. Furthermore, as in Example 14 of the "Training Materials," the specification of the present invention provides procedures for making proteins with substitutions, deletion, insertions, and additions. Accordingly, the present invention is analogous to that described in Example 14, and

thus, following the analysis provided in the Example 14, the invention of claims 37-46 and 54-57 is sufficiently described.

For these reasons, the rejection of claims 37-46 and 54-57 under 35 U.S.C. §112, first paragraph, for lack of written description should be reversed.

## CONCLUSION

In view of the arguments presented above, Appellants contend that each of claims 3, 5, and 6 is patentable. Therefore, reversal of the rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first and second paragraph, is respectfully solicited.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Box AF, Commissioner for Patents, Washington, DC 20231 on November 25, 2002.

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